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SPECIFIC LESIONS OF THE LUNGS IN ESPECIALLY  
DANGEROUS AND CERTAIN LITTLE KNOWN INFECTIONS

by

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Subject Country: USSR

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Medical publications contain many works devoted to acute pneumonia which occurs during very serious and some little known infections (glanders, melioidosis, deep-seated mitosis and others); however, practicing physicians are not sufficiently familiar with the specific inflammations of the lungs, since data on them are published in various journals. In this article, materials are summarized in the foreign literature regarding the basic clinical and diagnostic indicators of pneumonia.

Glanders occurs in man usually in the acute or in the chronic form as a septic disease with occurrence of numerous ulcers and abscesses in the internal organs and in the muscles, with development of secondary pneumonia. However, in aerogenous infections there may occur primary forms of pulmonary glanders. The incubation period varies from 3 to 5

days. The illness begins acutely, there appear symptoms of general intoxication, chills, the temperature rises to 39-40°C. A dry cough disturbs the patient from the first days of illness. Rhinitis with development of a thick mucus seldom develops. A pustular eruption appears on the face. As a result of hemoglobinous spread, there occur ulcers on the skin, abscesses in the muscles, and inflammations of the joints. At this time, signs of pneumonia appear. The pulse increases, there appears expectoration, sometimes blood stains. In the lower portions of the lungs are heard moist rumbling sounds. The recognition of secondary glanders pneumonia is made easier by the presence of other manifestations of the disease. The diagnosis of primary pneumonia which may occur through infections of the respiratory pathways is more difficult. The pulmonary form of glanders has been described by American authors Howe and Miller (1947), who observed six cases of aerogenous laboratory infections. Two individuals became infected with a strain of the infecting agent of low virulence. The illness took place in them without pronounced clinical manifestations with no great fever and with symptoms of general intoxication which were not severe. The lung infections were demonstrated only by means of X-rays. The other laboratory workers were infected with the virulent strain. The illness began in them with a chill, high fever, and pronounced general intoxication. The cough and expectoration were not remarkable. The skin infections and infections of the mucus membranes were not present. The changes seen in the X-ray were reminiscent of the early stages of lung abscesses. There were no deaths and no recurrences of the disease.

Until recently melioidosis was regarded as a rare disease with a high rate of mortality. It is endemic in regions of Southeast Asia, the Caribbean Sea and Australia (Johnson, 1967). It was recently established that antibodies to the causative organisms are found in the serum of 7-10% of the population of the endemic regions, which indicate the widespread dissemination of the infection (Nigg, 1963). The American physicians, Spotnitz, Rudnitzky and Rambaud (1967) described 9 cases of the pulmonary form of melioidosis. Of these individuals 8 were admitted to military hospitals with a diagnosis of pulmonary tuberculosis. In one case the illness began suddenly with shaking chills, elevation of temperature of the body to 40°C, and general weakness; in the others it began in a less acute manner. The temperature reached 38-40°C with great daily variations; the general condition was satisfactory. The complaints were pain in the chest, sometimes very severe, cough and expectoration, less frequently blood streaked sputum. The illness tended to have a prolonged course. The patients lost from 5-22.7 kg.

In portions of the infected lungs (usually the upper lobes) moist rumbling sounds could be heard. X-ray changes which were seen were quite reminiscent of the changes of tuberculosis. In 7 patients cavities formed very early and were already found at the time of the first X-ray examination during the acute period of the disease. The cavities had thin walls, and their size varied from 1-4 cm. In contrast to tuberculosis, pleural reaction was absent. A moderate leucocytosis (10,000-15,000) and an elevation of the erythrocyte sedimentation rate were noted. Similar illnesses were described in South Vietnam by Dong Hong Mo and Tran-Hiep-Cuong (1967). Dourox (1965) followed the pulmonary form of melioidosis in five soldiers (4 of these became infected in Vietnam), one of whom died. An autopsy microabscesses of the lungs were found. The pulmonary forms differ considerably from the previously described severe septic forms which usually took place in severely debilitated individuals. Out of 83 patients observed (Stanton and Fletcher, 1932) prior to the discovery of antibiotics only two survived. Even with the active use of antibiotic therapy these illnesses not infrequently had a lethal outcome.

Septic manifestations are absent in the pulmonary form. The illness has a benign course and responds well to antibiotic therapy. The best effect is obtained from preparations of the tetracycline group and chloramphenicol (Brockelmann, 1961). Apparently these forms of the disease are more widely distributed in regions endemic for melioidosis and they pass under the guise of other diagnoses. The pulmonary forms of the disease are diagnosed on the basis of characteristic clinical manifestations and are confirmed in the laboratory by the isolation of the causes of organisms from the sputum. The immunofluorescent method appears to be a like possibility (Biegeleisen et al, 1964), and the accompanying fixation reaction and the hemagglutination reaction have less significance for specific diagnosis.

Anthrax appears more often in dermatologic form and less often in the pulmonary and enteric. Thus, according to the data of Brachman (1966), in the United States from 1955 to 1965, out of 197 cases of anthrax only 8 patients had the pulmonary form. Even with modern methods of treatment the illness had a severe course, (7 out of 8 patients died, which apparently is due to the causative organisms ability to produce a toxin (Haines et al, 1965). In animal experiments it was established that the spores of the causative organisms which reach the lungs are rapidly phagocytosed by the alveolar macrophages (Shafa et al, 1966) and in the course of the first few days they caused a reaction in the tracheal bronchial lymphatic nodes (Vancurik, 1966).

The pulmonary form of anthrax begins acutely with a shaky chill an elevation of temperature of the body to 40°C and higher. There appear lachrymation, a marked hyperemia and swelling of the conjunctiva, sneezing, runny nose, hoarseness and cough. The conditions of the patient rapidly deteriorates; there is also shortness of breath, sharp pains in the back and cyanosis. The cough increases, there appear serous-hemorrhagic secretions which often coagulate ("raspberry jelly"), bronchitis, the picture of pneumonia develops, more often lobar, and sometimes also pleural effusion. Tachycardia and hypotonia supervene. The patients die from infectious collapse (often on the 2nd-4th day of the illness). In making a diagnosis there are considered the state of the epidemic, pronounced inflammation of the conjunctiva and of the upper respiratory tract, progressive increase in the severity of the disease. The isolation of the causative organisms in the sputum of the patient serves as the laboratory confirmation of the diagnosis. The results of the investigation are speeded by the use of the immuno-fluorescent method (Franeck, Kubin, 1967).

The plague often takes place with infection of the lungs. Such patients are most dangerous to those around them. Primary pulmonary plague takes place by means of aerogenous infection and has a particularly severe course (earlier all patients died in the course of 2-4 days). It is characterized by a sudden onset, rapid elevation of temperature, chills and vomiting. After the initial period of elevation of temperature the patients become depressed and slowed down; they complain of cutting pains in the chest, sometimes of pains in the upper gastric regions, and cough. The amount of sputum is quite variable. It is of a thick consistency, at first frothy and clear, then it becomes blood-tinged. On physical examinations there appear signs of lobular and pseudolobar pneumonia. The changes in the lungs are not proportional to the severity of the illness. The condition of the patient rapidly deteriorates, intoxication increases, shortens the breath (up to 40-50 respirations per minute), cyanosis, tachycardia, suppression of tonus. With the use of prophylactic antibiotics (streptomycin) the illness may take a course and only the isolation of the causative agents of plague from the sputum permits an explanation of its nature.

Pneumonia caused by chlamydozoans. With the exception of the widely distributed ornithosis which has a relatively benign course (mortality less than 1%), the causative factors of the chlamydozoan group can cause more severe illnesses (the pneumonia of San Francisco, Louisiana, Illinois), which are very little known to military physicians.

San Francisco pneumonia was observed in the city of this same name in 1940 by Eaton et al, (1941). At the beginning an adult man became sick with a severe bronchial pneumonia characterized by generalized intoxication, involvement of the pleura, and the development of infectious collapse. The patient died on the 17th day following the onset of the illness. In the course of 17-19 days 3 nurses became sick who took care of

the patient. The illness at first was reminiscent of the grippe; later the symptoms of intoxication came on, and infection of the lungs supervened. With the appearance of general intoxication two nurses died and the third recovered after a prolonged period of convalescence. It was possible to isolate from the patients an agent (strain SF), belonging to the group of ornithosis-lymphogranuloma.

Louisiana pneumonia was described by Olson and Treuting in 1944. In all there were 19 patients. The illness was characterized by the development of symptoms of pneumonia with a background of severe generalized intoxication. 8 of these individuals, which belongs to the group ornithosis-lymphogranuloma. The reservoir of the causative factor in nature was not known for a long time until in 1952 Schmid isolated it from the white heron.

Illinois pneumonia. An outbreak of severe pneumonia with lethal outcome (on the 15-18th day of illness) was observed in 1944 in Chicago (Zichis et al; 1945). There were instances of infection from individual to individual. An agent of the chlamydozoan group was isolated from the patients.

All the above noted 3 agents are completely related by biological characteristics (they have only small antigenic differences) and they produce illnesses in man which have a similar course. They (as well as ornithosis) have a course which has infection of the lungs but are distinguished by a very severe course and obvious predominance of symptoms of intoxication overt and pulmonary changes, the development of infectious collapse, and the possibility of person-to-person infection. Although the illnesses caused by these agents have not been recorded since, it is necessary to consider the possibility of their recurrence. The diagnosis is established on the basis of the isolation of the causative organisms (infection of mice, embryos, tissue cultures) or on the basis of serologic investigations (complement fixation reaction with ornithosis antigen).

Infection of the lungs is often observed in deep-seated micoses.

Histoplasmosis is widely distributed in the countries of South and North America (Papagianis, 1967), occasional cases being recorded also in other lands. The soil appears to be the natural reservoir of the fungus, particularly when polluted with the excreta of birds and bats. Infection in man takes place as a result of inhalation of the dust. The illness is characterized by protean clinical manifestations, but the pulmonary forms of histoplasmosis predominate (Proknow, 1967). Epidemics

are described during which all patients were observed to have infection of the lungs (Tosh et al, 1966).

The duration of the incubation period is almost 2 weeks. The illness begins acutely with elevation of temperature to 39°C and higher, and symptoms of general intoxication. A dry cough appears early as well as sticking pains in the chest. Physical examination does not reveal signs of illness, or the signs are quite scant. X-ray examination shows many small infiltrates or the picture of disseminated nodular infections of the lungs which remain between the course of 2-3 months. In the course of several years there may appear in their place numerous small calcifications. In severe but disseminated forms of histoplasmosis, besides the lungs, other organs are infected -- the liver, spleen, lymph glands (Saliba and Anderson, 1967), the mucus membrane of the mouth and throat (Bennett, 1967), pericardium (Rigel, Schriver, 1967), and eyes (Schlagel, 1967).

The diagnosis of histoplasmosis is based on epidemiological data (time spent in an endemic area) and clinical manifestations. In the laboratories the diagnosis is substantiated by means of the isolation of the fungus (from the sputum, blood and infected organs), complement fixation test with the antigen of histoplasmosis and histoplasmin skin test. It should be taken into consideration that in residents of endemic areas the skin test is often positive; for instance, in the United States it is positive in 30% of residence.

Coccidioidomycosis is endemic in the United States and in the countries of South America (Roberts, 1967). It has been described in Africa, Italy, the USSR and other countries. The fungus grows in the soil. The infection of man takes place of the result of the inhalation of the spores, which are carried by the wind. Laboratory infections have been described. The primary disease may take place asymptotically or in the form of a mild acute respiratory illness. Sometimes pneumonia takes place whose course may be fairly severe. The incubation period lasts 8-12 days. The illness begins acutely with fever, symptoms of general intoxication, pains in the joints, increased sweating, pains in the chest, cough and expectoration, sometimes bloody. Scattered dry rumbling can be heard. In the initial period of the disease X-ray examination shows single or multiple infiltrations, which are reminiscent of those of pneumonia. Not infrequently the bronchial lymph glands and sometimes the pleura are involved. Later on, thin-walled cavities of up to 4 cm in diameter may form in the place of the separate foci. The reaction of the surrounding tissue (if there are no bacterial complications) are almost always absent. These cavities may close spontaneously and recur (Salkin, 1967). Sometimes they lead to the formation of a bronchial-pleural fistula, pneumothorax, and empyema. In the course of the later development of the disease there may be noted bronchoectases

and fibrosis of the lungs. In severe disseminated forms of toxicoidiomycosis the fungus is carried throughout the whole body, causing meningitis, infection of the bones and joints, subcutaneous infiltrates, and abscesses. These forms often (up to 50%) have a fatal outcome.

The clinical diagnosis of coccidioidomycosis is difficult. The subcutaneous tests with coccidioidom serve as confirmatory evidence. It becomes positive already in the course of the first week in 85%, and at the end of the second week in all patients. The complement fixation test with coccidioidin antigen has a less significant meaning. The isolation of the spherules of the fungus in the sputum, the virulent material from the abscesses and the fistula is diagnostic.

Nocardiosis has been recorded in a number of countries (the United States, Australia, Germany, Czechoslovakia and others). The soil appears to be the reservoir of the causative factor. The infection takes place aerogenously and through the infected skin. The illness has a severe course, not infrequently with infection of the lungs. The generalized forms more often end fatally. The fever of nocardiosis is of the irregular type with large daily variations. It may continue for many weeks and is accompanied by chills and sweating. Weakness increases and not infrequently a hemolytic anemia develops (Gydell, 1965). The patient develops a cough which may be dry or may be accompanied by the production of virulent sputum (up to 200 cc in 24 hours). Severe pleural pain may be added. Sometimes atelectases may develop. X-rays show numerous round infiltrates. Later cavities form in their place. The hilar lymph nodes are enlarged. The clinical diagnosis is difficult. It is necessary to differentiate from other deep-seated mycoses (especially actinomycosis), cancer of the lung, (when atelectasis develops). The diagnosis is confirmed by the isolation of the causative organism from the sputum of the patient and from the organs of those who died.

Aspergillosis is more often superimposed on other chronic diseases of the lungs (tuberculosis, bronchial asthma among them) and on bacterial pneumonia (Keller et al; 1966). Sometimes primary pulmonary aspergillosis occurs, which in its manifestations differs little from acute bronchitis, catarrh of the respiratory tract and pneumonia. In acute bronchopulmonary aspergillosis there is fever, chills, nocturnal sweating, asthenia, loss of weight, cough with abundant viscous sputum, and pleural pain. Moist rumbles may be heard over the infected portions of the lungs as well as pleural rub; in the sputum there appears a mixture of blood and peculiar purulent lumps. Under the microscope, one sees accumulations of the fungus. The changes in the X-ray are characteristic. The process usually localizes in the upper portions where round infiltrates appear and later cavities with a broad surrounding band of infiltration around them. The diagnosis is confirmed by the isolation of the causative organisms from the sputum, the complement fixation test and the precipitant reaction with the specific antigen, as well as by the specific intracutaneous test.

The differential diagnosis of the above-described infections of the lungs is quite complicated since they have much in common in their clinical symptomatology (expressed by toxicosis, blood-streaked sputum, the formation of cavities in the lungs and so on), and physicians do not have the experience in observing the given illnesses. The duration of the incubation period may have some differential diagnostic significance. Some of the illnesses described have a short incubation period (plague -- 102 days, anthrax -- 2-5 days, glanders up to 3-5 days), the remainder are more prolonged (7-14 days and more). The contagiousness of the illnesses has to be taken into consideration (very high in pulmonary plague, moderate in illnesses due to chloredoans, and insignificant in glanders, melioidosis, and deep-seated mycoses). The character of the infection of other organs (besides the lungs) has an important diagnostic significance. For instance, the formation of pustules and subcutaneous abscesses in glanders and melioidosis, infection in bones and joints, in coccidioidomycosis, infection of the eyes in histoplasmosis, marked conjunctivitis in connection with infection of the upper respiratory tract with anthrax. Generalized intoxication is very pronounced in glanders and anthrax and somewhat weaker in other illnesses. Fatal outcomes occur in various periods: in glanders in the first 2 days, in anthrax in the 2-5 day, in illnesses caused by chlamydoans on 12-18 day, and the rest in a much longer period.

The changes in the lungs also have peculiarities. The sputum in pulmonary glands and anthrax may be almost pure blood, but in the other illnesses blood appears in the form of filaments. In mycosis the virulent sputum may contain peculiar lumps which contain the fungus. In the pulmonary form of glanders, anthrax, and pneumonia caused by chlamydoans, massive infiltrates are formed without a tendency to lysis. In mycosis and melioidosis there are numerous infiltrates, most often located in the upper portions of the lungs. In melioidosis thin-walled cavities are formed in the lungs without the pleural reaction. In mycosis the pleura is involved in the process, histoplasmosis usually is not resolved, aspergillosis is characterized by the formation of cavities in the lungs with a broad band of infiltration around them. The final diagnosis is established after the isolation of the causative factor or by obtaining the results of serologic reactions or allergic tests.